

IN THE CLAIMS:

Please cancel claims 125-129, 156 and 157, add new claims 433-465, and amend the claims shown below.

1-124. (Previously cancelled)

125-129. (Currently cancelled)

130-155. (Previously cancelled)

156-157. (Currently cancelled)

158. (Currently amended) An aggregate probe[, the aggregate probe] comprising at least two types of nanoparticles having oligonucleotides attached thereto, the nanoparticles of the aggregate probe being bound to each other as a result of the hybridization of some of the oligonucleotides attached to them, at least one of the types of nanoparticles of the aggregate probe having oligonucleotides attached thereto which have a sequence complementary to a portion of the sequence of a nucleic acid.

159. (Currently amended) [The] An aggregate probe [of Claim 158] comprising at least two types of nanoparticles, each nanoparticle having at least two types of oligonucleotides attached thereto, the first type of oligonucleotides attached to each type of nanoparticles having a sequence complementary to a portion of the sequence of a nucleic acid, the second type of oligonucleotides attached to the first type of nanoparticles having a sequence complementary to at least a portion of the sequence of the second type of oligonucleotides attached to the second type of nanoparticles.

160. (Currently amended) [The] An aggregate probe [of Claim 158] comprising at least three types of nanoparticles having oligonucleotides attached thereto, at least a portion of the oligonucleotides attached to the first type of nanoparticles having a sequence complementary to at least a portion of the sequence of the oligonucleotides attached to the second type of nanoparticles, the at least a portion of the oligonucleotides attached to the second type of nanoparticles having a sequence complementary to at least a portion of the sequence of the

oligonucleotides attached to the first type of nanoparticles, and the third type of nanoparticles having at least two types of oligonucleotides attached thereto, the first type of oligonucleotides having a sequence complementary to a portion of the sequence of a nucleic acid, and the second type of oligonucleotides having a sequence complementary to at least a portion of the sequence of the oligonucleotides attached to the first or second type of nanoparticles.

161. (Currently amended) An aggregate probe[, the aggregate probe] comprising at least two types of nanoparticles having oligonucleotides attached thereto, the nanoparticles of the aggregate probe being bound to each other as a result of the hybridization of some of the oligonucleotides attached to them, at least one of the types of nanoparticles of the aggregate probe having oligonucleotides attached thereto which have a hydrophobic group attached to the end not attached to the nanoparticles.

162-432. (Previously cancelled)

433. (New) The aggregate probe of any one of claims 158-161 wherein the oligonucleotides are attached to the nanoparticles in a stepwise ageing process comprising (i) contacting the oligonucleotides with the nanoparticles in a first aqueous solution for a period of time sufficient to allow some of the oligonucleotides to bind to the nanoparticles; (ii) adding at least one salt to the first aqueous solution to create a second aqueous solution; and (iii) contacting the oligonucleotides and nanoparticles in the second aqueous solution for an additional period of time to enable additional oligonucleotides to bind to the nanoparticles.

434. (New) The aggregate probe of Claim 433 wherein the second aqueous solution has an ionic strength sufficient to overcome at least partially the electrostatic attraction or repulsion of the oligonucleotides for the nanoparticles and the electrostatic repulsion of the oligonucleotides to each other.

435. (New) The aggregate probe of Claim 433 wherein the oligonucleotides and nanoparticles are contacted in aqueous solution for about 12 to about 24 hours.

436. (New) The aggregate probe of Claim 433 wherein salt is added to the aqueous solution to form the aqueous salt solution which is buffered at pH 7.0 and which contains about 0.1 M NaCl.

437. (New) The aggregate probe of Claim 433 wherein the oligonucleotides and nanoparticles are contacted in the aqueous salt solution for an additional 40 hours to increase the density of oligonucleotides bound to the nanoparticles.

438. (New) The aggregate probe of Claim 436 wherein the salt is added to the first aqueous solution in a single addition.

439. (New) The aggregate probe of Claim 436 wherein the salt is added gradually to the first aqueous solution over time.

440. (New) The aggregate probe of Claim 436 wherein the salt is selected from the group consisting of consisting of sodium chloride, magnesium chloride, potassium chloride, ammonium chloride, sodium acetate, ammonium acetate, a combination of two or more of these salts, one of these salts in a phosphate buffer, and a combination of two or more these salts in a phosphate buffer.

441. (New) The aggregate probe of Claim 440 wherein the salt is sodium chloride in a phosphate buffer.

442. (New) The aggregate probe of any one of claims 158-161 wherein the oligonucleotides are present on a surface of the nanoparticles at a surface density of at least 10 picomoles/cm².

443. (New) The aggregate probe of Claim 442 wherein the oligonucleotides are present on the surface of the nanoparticles at a surface density of at least 15 picomoles/cm².

444. (New) The aggregate probe of Claim 443 wherein the oligonucleotides are present on the surface of the nanoparticles at a surface density from about 15 picomoles/cm² to about 40 picomoles/cm².

445. (New) The aggregate probe of any one of claims 158-161 wherein the nanoparticles are metal nanoparticles or semiconductor nanoparticles.

446. (New) The aggregate probe of Claim 445 wherein the nanoparticles are gold nanoparticles.

447. (New) The aggregate probe of any one of claims 158-161 wherein at least some of the oligonucleotides on the nanoparticles comprise at least one type of recognition oligonucleotides, each type of recognition oligonucleotides comprising a spacer portion and a recognition portion, the spacer portion being designed so that it is bound to the nanoparticles, the recognition portion having a sequence complementary to at least a portion of a sequence of the target nucleic acid.

448. (New) The aggregate probe of Claim 447 wherein the spacer portion has a moiety covalently bound to it, the moiety comprising a functional group through which the spacer portion is bound to the nanoparticles.

449. (New) The aggregate probe of Claim 447 wherein the spacer portion comprises at least about 10 nucleotides.

450. (New) The aggregate probe of Claim 449 wherein the spacer portion comprises from about 10 to about 30 nucleotides.

451. (New) The aggregate probe of Claim 447 wherein the bases of the nucleotides of the spacer portion are all adenines, all thymines, all cytosines, all uracils or all guanines.

452. (New) The aggregate probe of any one of claims 158-161 wherein at least some the oligonucleotides bound to the nanoparticles comprise at least one type of recognition oligonucleotides, each type of recognition oligonucleotides comprising a sequence complementary to at least one portion of a sequence of the target nucleic acid; and a type of diluent oligonucleotides.

453. (New) The aggregate probe of Claim 452 wherein, each type of recognition oligonucleotides comprises a spacer portion and a recognition portion, the spacer portion being designed so that it is bound to the nanoparticles, the recognition portion having a sequence complementary to at least one portion of a sequence of the target nucleic acid.

454. (New) The aggregate probe of Claim 453 wherein the spacer portion has a moiety covalently bound to it, the moiety comprising a functional group through which the spacer portion is bound to the nanoparticles.

455. (New) The aggregate probe of Claim 453 wherein the spacer portion comprises at least about 10 nucleotides.

456. (New) The aggregate probe of Claim 455 wherein the spacer portion comprises from about 10 to about 30 nucleotides.

457. (New) The aggregate probe of Claim 453 wherein the bases of the nucleotides of the spacer portion are all adenines, all thymines, all cytosines, all uracils or all guanines.

458. (New) The aggregate probe of Claim 453 wherein the diluent oligonucleotides contain about the same number of nucleotides as are contained in the spacer portions of the recognition oligonucleotides.

459. (New) The aggregate probe of Claim 458 wherein the sequence of the diluent oligonucleotides is the same as that of the spacer portions of the recognition oligonucleotides.

460. (New) The aggregate probe of any one of claims 158-161 wherein the oligonucleotides are bound to the nanoparticles through sulfur linkages.

461. (New) A kit comprising any one of the aggregate probes of claims 158-161.

462. (New) The kit according to claim 461, further comprising a substrate having oligonucleotides bound thereto.

463. (New) The kit according to claim 462, wherein the substrate has a plurality of oligonucleotides attached there to in an array to allow for the detection of multiple portions of a single nucleic acid, the detection of multiple different nucleic acids, or both.

464. (New) A kit comprising:

a substrate, the substrate having oligonucleotides attached thereto, the oligonucleotides having a sequence complementary to the sequence of a first portion of a nucleic acid;

a first container holding liposomes having oligonucleotides attached thereto which have a sequence complementary to the sequence of a second portion of the nucleic acid; and

a second container holding an aggregate probe comprising at least two types of nanoparticles having oligonucleotides attached thereto, the nanoparticles of the aggregate probe being bound to each other as a result of the hybridization of some of the oligonucleotides attached to them, at least one of the types of nanoparticles of the aggregate probe having oligonucleotides attached thereto which have a hydrophobic group attached to the end not attached to the nanoparticles.

465. (New) A kit comprising a container holding an aggregate probe, the aggregate probe comprising at least two types of nanoparticles having oligonucleotides attached thereto, the nanoparticles of the aggregate probe being bound to each other as a result of the hybridization of some of the oligonucleotides attached to them, at least one of the types of nanoparticles of the aggregate probe having oligonucleotides attached thereto which have a hydrophobic group attached to the end not attached to the nanoparticles.